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10/069,999	03/01/2002	Takashi Kawasuji	2002_0288A	5732

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EXAMINER

EPPERSON, JON D

ART UNIT PAPER NUMBER

1639

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/069,999

Applicant(s)

KAWASUJI ET AL.

Examiner

Jon D. Epperson

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 1-6 and 15-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7,8 and 10-14 is/are rejected.
- 7) ☒ Claim(s) 9 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 2/17; 3/1; 3/26.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Status of the Application***

1. The Response filed February 17, 2006 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

***Status of the Claims***

3. Claims 1-23 were pending. Applicants canceled claim 24 and amended claims 1, 5-14 and 17-23. No claims were added. Therefore, claims 1-23 are currently pending.
4. Claims 1-6 and 15-23 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.
5. Therefore, claims 7-14 are examined on the merits in this action.
6. Please note that this application contains claims 1-6 and 16-23 drawn to a nonelected invention(s). This was addressed in the previous action (see 10/17/05 Non-final Office Action, paragraph 3). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

### **Withdrawn Objections/Rejections**

7. All rejections are withdrawn in view of Applicants' arguments and amendments to claims 7-14. Specifically, Applicants removed the improper dependency in claims 9-14 that was objected to. Furthermore, Applicants removed the "prodrug" that was rejected under 35 U.S.C. 112, first paragraph. Applicants also removed the "has a bond at" language that was rejected under 35 U.S.C. 112, second paragraph. Applicants amendment to remove Z as "optionally substituted alkyl" also overcomes the Ogura et al. rejection under 35 U.S.C. 102(b). Finally, Applicants arguments (on pages 10 and 11) overcome the Thomson et al. rejection under 35 U.S.C. 102(b) because the  $C(Z)=C(X)Y$  is not adjacent to the heteroatom in the ring (A).

### **New Rejections**

#### ***Claim Rejections – 35 U.S.C. 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 8**, the term "combined with" is vague and indefinite. For example, it is not clear how the heteroaryl is being combined with an atom adjacent to a heteroatom in Y? Is the entire heteroaryl combined with such an atom (e.g., like a metallocene) or is some select atom within the heteroaryl combined with an adjacent atom? Furthermore,

Art Unit: 1639

wouldn't the ring structure necessarily combine with an adjacent atom to form the ring?

If so, how does this language further limit the claim? Applicants are requested to clarify and/or correct. Therefore, claims 8 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

***Claims Rejections - 35 U.S.C. 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claim 8 was amended in the 2/17/06 Response. However, applicant did not show where support for this amendment could be found in the specification. For example, Applicants' current claims read on "sandwich" type compounds, metallocenes, wherein an adjacent atom, say a metal, is combined with the  $\pi$  orbitals of the conjugated organic ring (see 35 U.S.C. 112, second paragraph rejection above). If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02. Therefore, claim 8 and all dependent claims are rejected under 35 U.S.C. 112, first paragraph for containing new matter.

***Claims Rejections - 35 U.S.C. 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 7, 10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Masquelin et al. (Masquelin, et al. "Synthesis of enantiomerically pure D- and L-(heteroaryl)alanines by asymmetric hydrogenation of (Z)- $\alpha$ -amino- $\alpha,\beta$ -didehydroesters" *Helvetica Chimica Acta* **1994**, 77(5), 1395-411).

For ***claims 7, 10 and 13***, Masquelin et al. (see entire document) disclose, for example, 2-[3-methoxy-3-oxo-3-[[-(phenylmethoxy)carbonyl]amino]-1-propenyl]-,1,1-dimethylethylester, 1H-Pyrrole-1-carboxylic acid (see Masquelin et al., page 1396, Scheme 1, R = 1-Boc-1H-pyrrol-2-yl; see also page 1401, scheme 3, entries 1 and 2; RN 161282-31-1), which anticipates the claimed invention. In this scenario, R<sup>1</sup> = *t*-butyl (i.e., optimally substituted branched alkyl), Z<sup>3</sup>/Z<sup>1</sup> = bond, Z<sup>2</sup> = -C(=O)-O-, A = pyrrole (i.e., an optionally substituted aromatic heterocycle), Z = hydrogen, Y = -C(=R<sup>2</sup>)-R<sup>3</sup>-R<sup>4</sup> wherein R<sup>2</sup>/R<sup>3</sup> = oxygen and R<sup>4</sup> = methyl (i.e., optionally substituted alkyl), and X = NH-C(=O)-O-CH<sub>2</sub>-Ph (i.e., an optionally substituted amino). The -C(Z)=C(X)Y groups is also adjacent to the pyrrole ring nitrogen.

Art Unit: 1639

11. Claims 7, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Noda et al. (EP 0 696 586 A1) (Date of Patent is **February 14, 1996**).

For *claims 7, 12 and 13*, Noda et al. (see entire document) disclose methyl 2-benzyloxycarbonylamino-3-[5-(10hexahydroazepinylmethyl)-2-thienyl]propenoate (e.g., see page 22, Example 39, RN 166812-32-4P), which anticipates the claimed invention. In this scenario, R<sup>1</sup> = hexahydroazepinyl (i.e., optionally substituted non-aromatic heterocyclic group), Z<sup>3</sup>/Z<sup>1</sup> = bond, Z<sup>2</sup> = -CH<sub>2</sub>- (i.e., an alkylene), A = thiophene (i.e., an optionally substituted aromatic heterocycle), Z = hydrogen, Y = -C(=R<sup>2</sup>)-R<sup>3</sup>-R<sup>4</sup> wherein R<sup>2</sup>/R<sup>3</sup> = oxygen and R<sup>4</sup> = methyl (i.e., optionally substituted alkyl), and X = NH-C(=O)-O-CH<sub>2</sub>-Ph (i.e., an optionally substituted amino). The -C(Z)=C(X)Y groups is also adjacent to the thiophene ring nitrogen.

### ***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

Art Unit: 1639

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 7, 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noda et al. (EP 0 696 586 A1) (Date of Patent is **February 14, 1996**) in view of Patani et al. (Patani, G. A.; LaVoie, E. J. "Bioisosterism: A Rational Approach in Drug Design" *Chem. Rev.* **1996**, *96*, 3147-3176 ).

For *claims 7, 12 and 13*, Noda et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 7, 12 and 13.

The prior art teachings of Noda et al. differ from the claimed invention as follows:

For *claims 11 and 14*, Noda et al fail to teach the use of a pyridine ring. Noda et al. only teach the use of a thiophene ring.

However, Patani et al. teach the following limitations that are deficient in Noda et al.:

For *claims 11 and 14*, Patani et al. (see entire document) teach the use of isosteric replacements including thiophene → pyridine in order to produce compounds with more favorable physicochemical properties e.g., better bioavailability, less side effects, increased potency, etc. (e.g., see Patani et al., Introduction; see also page 3158, section E, "Ring Equivalents", especially column 1, paragraph 1, "The use of the classical



Art Unit: 1639

bioisosteres benzene, thiophene and pyridine resulted in analogues with retention of biological activity within different series of pharmacological agents”).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the thiophene → pyridine substitution as taught by Patani et al. using the thiophene molecules as disclosed by Noda et al. because Patani et al. explicitly state that these two ring systems are functionally “equivalent” and are routinely used to produced analogues for pharmacological lead modification (e.g., see MPEP § 2144.09 “An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties.” *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991)). Furthermore, a person of skill in the art would have been further motivated to make this thiophene → pyridine substitution because Patani et al. explicitly state that favorable medicinal properties can be achieved using these bioisosteric ring substitutions (e.g., see Patani, page 3158, Section E; see also page 3147, paragraph 1, “Bioisoserism [i.e., the thiophene → pyridine substitution] represents one approach used by the medicinal chemist for the rational modification of lead compounds into safer and more clinically effective agents”). Finally, a person of ordinary skill in the art would reasonably have expected to be successful because the thiophene → pyridine substitution represents a “classic” bioisosteric lead modification that has general utility in a wide range of systems (e.g., see page 3158, section E, “Ring Equivalents”, especially column

Art Unit: 1639

1, paragraph 1, "The use of the classical bioisosteres benzene, thiophene and pyridine resulted in analogues with retention of biological activity within different series of pharmacological agents [i.e., a wide range of systems]").

### ***Allowable Subject Matter***

15. Claim 9 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Conclusion***

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 10/069,999

Page 10

Art Unit: 1639

Jon D. Epperson, Ph.D.

May 6, 2006

JON EPPERSON, PH.D.  
PATENT EXAMINER

A handwritten signature in black ink, consisting of a large, stylized 'J' followed by a long, sweeping horizontal line that extends to the right.